

### **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of Claims:**

Claims 1-29 (cancelled)

30. (New) Polypeptide having a  $\beta$ -secretase type activity, wherein said polypeptide is able to specifically cleave the natural precursor (APP) of the  $\beta$ -amyloid peptide.

31. (New) Polypeptide according to claim 30, wherein the amyloid peptide precursor (APP) does not carry any mutation in its protein sequence.

32. (New) Polypeptide according to claim 30, which has been purified from human cells from an individual who is not suffering from Alzheimer's disease.

33. (New) Polypeptide according to claim 30, which:

- possesses a molecular mass of about 70 kDa,
- possesses an isoelectric point of about 6.0,
- is an endopeptidase of the serine protease family,
- is an endopeptidase of the chymotrypsinsensitive type,
- achieves a maximum activity at a pH of between 7 and 8.

34. (New) Polypeptide according to claim 30, wherein said activity does not depend on a second substrate and/or ligand.

35. (New) Polypeptide according to claim 30, wherein said activity does not depend on ions, preferably calcium or magnesium cations.

36. (New) Polypeptide according to claim 30, additionally comprising a signal sequence.

37. (New) Polypeptide according to claim 36, wherein said signal sequence is selected from the sequence of the signal peptide of IgkB, the signal peptide of APP and the signal peptides of the subunits, of the muscle and central nervous system nicotinic acetylcholine receptors.

38. (New) Pharmaceutical composition comprising a polypeptide according to any one of claims 30-37 as the active principle.

39. (New) Pharmaceutical composition according to claim 38 wherein said polypeptide is combined or with other active principles.

40. (New) Pharmaceutical composition according to claim 38 for at least partially inhibiting the interaction between said polypeptide and said  $\beta$ -amyloid peptide precursor and/or inhibiting the activity of said polypeptide.

41. (New) Pharmaceutical composition according to claim 38, for intervening in the metabolism of said  $\beta$ -amyloid peptide and, preferably, for inhibiting or retarding production of said  $\beta$ -amyloid peptide.

42. (New) Pharmaceutical composition according to claim 38, for treating neurodegenerative diseases, preferably, for treating Alzheimer's disease.

43. (New) Method for treating neurodegenerative diseases, in particular Alzheimer's disease, comprising a step of administering a polypeptide according to any one of claims 30-37 to a patient suffering from said disease.

44. (New) Method for purifying, from cells derived from individuals who are not suffering from Alzheimer's disease, a polypeptide according to any one of claims 30-37, wherein said method comprises the following steps:

- removing the supernatant from the cell culture and then concentrating it,
- concentrating the concentration product once again on a tangential membrane,

- purifying the resulting product by means of consecutive steps of chromatography, in particular by means of steps of exclusion chromatography, ion exchange chromatography and hydrophobic interaction chromatography.

45. (New) Method for producing a polypeptide according to any one of claims 30-37, wherein said method uses a human cell line, which represents the central or peripheral nervous system and the immune system and which is able to carry out the normal metabolism of said  $\beta$ -amyloid peptide precursor.

46. (New) Method according to claim 39, wherein the cell line is the monocyte-derived THP1 cell line (ATCC TIB 202).

47. (New) Antibody or antibody fragment directed against a polypeptide according to any one of claims 30-37, wherein said antibody or antibody fragment possesses the ability to at least partially inhibit the interaction between the said polypeptide and said  $\beta$ -amyloid peptide precursor and/or inhibit the activity of said polypeptide and/or intervene in the metabolism of said  $\beta$ -amyloid peptide.

48. (New) Pharmaceutical composition comprising at least one antibody fragment according to claim 47 as the active principle.

49. (New) Pharmaceutical composition according to claim 48, wherein said antibody or antibody fragment is combined with other active principles.

50. (New) Pharmaceutical composition according to claim 48, for at least partially inhibiting the interaction between said polypeptide and said  $\beta$ -amyloid peptide precursor and/or inhibiting the activity of said polypeptide.

51. (New) Pharmaceutical composition according to claim 48, for intervening in the metabolism of said  $\beta$ -amyloid peptide and, preferably, for inhibiting or retarding production of said  $\beta$ -amyloid peptide.

52. (New) Pharmaceutical composition according to claim 48, for treating neurodegenerative diseases, preferably for treating Alzheimer's disease.

53. (New) Method for treating neurodegenerative diseases, and in particular Alzheimer's disease, comprising a step of administering an antibody or antibody fragment according to claim 47 to a patient suffering from said disease.

54. (New) Compound which is either not exclusively peptide in nature, or is a non-peptide compound, said compound being able to cleave the  $\beta$ -amyloid peptide precursor at the  $\beta$ -secretase site and is obtained by duplicating the active motifs of the polypeptide according to any one of claims 30-37 with non-peptide structures or structures which are not exclusively peptide in nature.

55. (New) Method for detecting or isolating compounds which are able to at least partially inhibit the interaction of the polypeptide according to any one of claims 30-37 and the  $\beta$ -amyloid peptide precursor and/or inhibit the activity of said polypeptide, wherein said method comprises the following steps:

- a. bringing into contact a molecule or a mixture containing different molecules, which may not have been identified, with a recombinant cell expressing said polypeptide under conditions which would enable said polypeptide and said molecule to interact if the latter possessed an affinity for said polypeptide, and
- b. detecting and/or isolating the molecules which are bound to said polypeptide.

56. (New) Ligand for a polypeptide according to any one of claims 30-37, which can be obtained according to the method of claim 55.

57. (New) Ligand according to claim 56, wherein said ligand is an antagonist, an agonist or an inhibitor of said polypeptide.

58. (New) Pharmaceutical composition comprising at least one ligand according to claim 56 as the active principle.

59. (New) Pharmaceutical composition according to claim 58, wherein said ligand is an inhibitor of said polypeptide.

60. (New) Pharmaceutical composition according to claim 58, wherein said ligand is combined with other active principles.

61. (New) Pharmaceutical composition according to claim 58, which is intended for at least partially inhibiting the interaction between said polypeptide and said  $\beta$ -amyloid peptide precursor and/or inhibiting the activity of said polypeptide.

62. (New) Pharmaceutical composition according to claim 58, which is intended for intervening in the metabolism of said  $\beta$ -amyloid peptide and, preferably, for inhibiting or retarding production of said  $\beta$ -amyloid peptide.

63. (New) Pharmaceutical composition according to claim 58, which is intended for treating neurodegenerative diseases, preferably, for treating Alzheimer's disease.

64. (New) Method for treating neurodegenerative diseases, and in particular Alzheimer's disease, comprising a step of administering a ligand according to claim 56 to a patient suffering from said disease.

65. (New) Method for detecting compounds capable of inhibiting the interaction between the polypeptide according to claims 30-37 and its substrate, wherein said method uses a human cell line, which represents the central or peripheral nervous system and the immune system and which is able to carry out the normal metabolism of said  $\beta$ -amyloid peptide precursor.

66. (New) Method according to claim 65, wherein said cell line is the monocyte-derived THP1 cell line (ATCC TIB 202).

67. (New) Method for detecting molecules which modify the activity of a polypeptide according to claims 30-37, wherein said method comprises the following steps:

- bringing into contact a polypeptide which exhibits an activity of the  $\beta$ -secretase type according to claims 30-37 with a molecule or a mixture which contains different molecules, which may not have been identified,
- bringing into contact the reaction mixture from the preceding step with the substrate of said polypeptide, which substrate is preferably APP in its natural form,
- measuring said  $\beta$ -secretase activity on said substrate,
- detecting and/or isolating the molecules which modify said  $\beta$ -secretase activity of said polypeptide.

68. (New) Viral or plasmid vector containing the nucleotide sequences of agonists or antagonists of polypeptide according to claims 30-37, for transfecting said sequences into appropriate host cells and expressing said molecules in vivo, ex-vivo and/or in vitro.